CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-165

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	April 23, 2009
To:	Russell Katz, M.D., Director Division of Neurology Products
Through:	Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis, HFD-420
From:	Laura Pincock, RPh, PharmD, Acting Team Leader Division of Medication Error Prevention and Analysis, HFD-420
Subject:	Proprietary Name Review
Drug Name(s):	Cambia (Diclofenac Potassium) for Oral Solution 50 mg packet
Application Type/Number:	NDA 22-165
Applicant/Applicant:	ProEthic Pharmaceuticals, Inc.
OSE RCM #:	2008-1561

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Cambia, is not vulnerable to name confusion that could lead to medication errors. During this review we identified 27 names for their similarity to Cambia. The results of the Failure Mode Effects Analysis found that the proposed name, Cambia is not vulnerable to name confusion that could lead to medication errors with any of the 27 names. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Cambia.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product; DMEPA rescinds this Risk Assessment finding, and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Division of Neurology Products for an assessment of the proposed proprietary name, Cambia, regarding potential name confusion with other proprietary or established drug names in normal practice settings.

1.2 PRODUCT INFORMATION

Cambia is the proposed proprietary name for diclofenac powder for oral solution. Cambia is intended for the acute treatment of migraine attacks with or without aura in adults (18 years of age or older). Cambia is proposed to be marketed in single dose packets each containing 50 mg of diclofenac potassium powder for oral solution. The contents of the single packet are to be mixed with 1 to 2 ounces (30 to 60 mL) of water immediately prior to administration.

Cambia is proposed to be marketed in a carton of 9 packets (3 sets of 3 co-joined packets). Cambia should be stored at controlled room temperature (25˚C) with excursions permitted to 15˚C to 30˚C.

2 METHODS AND MATERIALS

This section describes the methods and materials used by DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus for the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Cambia, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA and ANDA products currently under review by the Agency.

For the proprietary name, Cambia, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). DMEPA normally conducts internal CDER prescription analysis studies and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.2). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[3]

2.1.1 Search Criteria

DMEPA staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

For this review, particular consideration was given to drug names beginning with the letter 'C' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[4,5]

To identify drug names that may look similar to Cambia, DMEPA staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (six letters), and upstrokes (two, capital letter 'C' and lower case letter 'b'). Additionally, several letters in Cambia may be vulnerable to ambiguity when scripted, including the capital letter 'C' may appear as capital letters 'A' or 'G'; lower case 'a' may look like lower case 'e' or 'i'; lower case 'm' may look like lower case 'n' or 'u' or 'r'; lower case letter 'b' may appear as lower case 'f' or 't'; lower case 'i' may appear as lower case 'e' or 'r'; and lower case 'a' may appear as lower case 'e' or 'o' or 'n'. As such, DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Cambia.

When searching to identify potential names that may sound similar to Cambia, DMEPA staff search for names with similar number of syllables (3), stresses (Cam-bi-AH or Cam-BI-ah), and placement of vowel and consonant sounds. Additionally, we consider that pronunciation of parts of the name can vary such as 'Cam-' may sound like 'Kim-'. The Applicant's intended pronunciation of the proprietary name, Cambia, could not expressly be taken into consideration, as this was not provided with the proposed name submission. Because names are often mispronounced and/or spoken with regional accents and dialects, other potential pronunciations of the names are considered.

The staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Cambia), the proposed established name (diclofenac potassium powder for oral solution), proposed indication (migraine headache), strength (50 mg), dose (50 mg), frequency of administration (one time), route (oral), and dosage form (powder for oral solution). Appendix A provides a more detailed listing of the product characteristics that DMEPA staff generally take into consideration.

Lastly, DMEPA staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and DMEPA staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Cambia, was provided to DMEPA staff to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Cambia using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some

[4] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[5] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 FDA Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Cambia. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the Division of Medication Errors Prevention and Analysis staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of DMEPA staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 CDER Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Cambia with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Cambia in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA staff.

Figure 1. Cambia Study (conducted on November 13, 2008)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: Cambia dissolve 1 packet in 1-2 ounces of water and drink as directed	" Cambia, Dispense 1 box, Dissolve 1 packet in 1-2 ounces of water and drink as directed"
Outpatient Prescription: Cambia Dissolve 1 packet in 1-2 oz. of Water and drink as directed #1 box	

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

[6] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Cambia convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Cambia to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary name. The threshold

set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, Joint Commission, and ISMP, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

The search of the internet, several standard published databases and information sources (see Section 7 References) yielded a total of 25 names as having some similarity to the name Cambia.

Nineteen of the 25 names were thought to look like Cambia. These include Combivir, Ambien/Ambien CR, Cimzia, (b) (4) Certiva, (b) (4), Combid, Cartia, Ambral, Campral, Cancidas, Cantil, Geodon, Combi Rx, (b) (4), Comtan, Aredia, and Camolea. Two of the 25 names were thought to sound like Cambia. These include Campath (b) (4) The remaining four names were thought to look and sound similar to Cambia (Camila, Avandia, (b) (4) and Cambogia).

Additionally, we did not identify any United States Adopted Names (USAN) stems in the name, Cambia, as of September 26, 2008.

3.1.2 Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1.1. above) and noted two additional names thought to have orthographic or phonetic similarity to Cambia. These names

were (b) (4) and (b) (4) The Expert Panel also noted that Cambia means "change" in Spanish. DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 FDA Prescription Analysis Studies

A total of 38 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Twenty nine of the participants interpreted the name correctly as "Cambia," with correct interpretation occurring in both the inpatient written studies (n=9) and the outpatient written studies (n=20). The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Cambia. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety Evaluator Risk Assessment

Twenty seven names were analyzed to determine if the drug names could be confused with Cambia and if the drug name confusion would likely result in a medication error. All of the identified names were determined to have some orthographic and/or phonetic similarity to Cambia, and thus determined to present some risk of confusion.

Failure mode and effect analysis was then applied to determine if the potential name, Cambia, could potentially be confused with any of the 27 names and lead to medication errors. This analysis determined that the name similarity between Cambia and the identified names was unlikely to result in medication errors with any of the 27 products identified for the reasons presented in Appendicies C-G.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

Our evaluation identified 27 names as having some similarity to the proposed name, Cambia. Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining 27 names and lead to medication errors. This analysis determined that the name similarity between Cambia was unlikely to result in medication errors with any of the 27 products for the reasons presented in Appendices C through G.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Cambia, is not vulnerable to name confusion that could lead to medication errors in the current marketplace. Thus we have no objections to the name, Cambia, for this product. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product; DMEPA rescinds this Risk Assessment finding, and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5.1 COMMENTS TO THE DIVISION

We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Daniel Brounstein, project manager, at 301-796-0674.

5.2 COMMENTS TO THE APPLICANT

5.2.1 Proprietary Name

We have completed our review of the proposed proprietary name, Cambia, and have concluded that it is acceptable.

The proposed proprietary name Cambia will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

6 REFERENCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

Drug Facts and Comparisons is a compendium organized by therapeutic course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

5. Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

Provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (www.statref.com)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.lexi.com)

A web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

DMEPA staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare the spelling of the proposed proprietary name with the proprietary and proper name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. DMEPA staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the

overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, DMEPA staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstokes Downstrokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

		Placement of consonant sounds Overlapping product characteristics	

Appendix B: **CDER Prescription Study Responses**

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Cambia	Cambia	Cambia
Cambia	Cambia	Cambia
Combia	Cambia	Candia
Cambria	Cambia	
Cambia	Cambid	
Cambria	Cambia	
Cambia	Combid	
Cambia	Cambia	
Cambia	Cambid	
Cambra	Cambia (none)	
	Cambia	
	Cambia	
	Cambia	

Appendix C: Product names that have not ever been marketed.

Proprietary Name	Similarity to Cambia	Status of product name
		(b) (4)
		(b) (4)

		also registered in Switzerland and Mexico.
		(b) (4)

Appendix D: Products withdrawn from the market.

Proprietary Name	Similarity to Cambia
Certiva (diphtheria and tetanus toxoids and acellular pertussis) Vaccine Adsorbed	Look
Combid Spansule (anti-spasmodic)	Look

Appendix E: Products marketed in foreign countries

Proprietary Name	Similarity to Cambia
(b) (4) (unknown pharmaceutical preparation in Switzerland but expired trademark)	Look
Ambral (metronidazole- S.Africa, no longer marketed)	Look

Appendix F: Products with no overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Cambia **(diclofenac potassium) for oral solution**	**N/A**	**50 mg**	**One packet (50 mg) mixed in 30-60 mL of water and then ingested**
Combivir (lamivudine/zidovudine)	Look	Tablets: 150 mg/300 mg	One tablet orally twice daily
Ambien **Ambien CR** (zolpidem)	Look	Tablet: 5 mg Capsule: 6.25 mg	One tablet or capsule ingested immediately before bedtime
Cimzia (certoluzimab)	Look	Powder for Injection: 200 mg Prefilled syringes***: 200 mg	400 mg via two 200 mg subcutaneous injections, repeat dose 2 and 4 weeks after initial dose. Maintenance: 400 mg every 4 weeks
Cartia XT (diltiazem)	Look	Capsules, Extended-release: 120 mg, 180 mg, 240 mg, 300 mg	One capsule orally once a day.
Campral **Campral Dose Pack** (acamprosate)	Look	Tablet, Enteric coated: 333 mg (180 count)	2 tablets (666 mg) taken three times a day (a lower dose may be effective in some patients).
Geodon (ziprasidone)	Look	Capsules: 20 mg, 40 mg, 60 mg, 80 mg Injection, Powder for Reconstitution: 20 mg	20 mg to 100 mg orally twice daily Via intramuscular injection: 10 mg every 2 hours or 20 mg every 4 hours (maximum: 40 mg/day). Oral therapy should replace intramuscular therapy as soon as possible
ComBi Rx (prenatal vitamin)	Look	Tablet: Calcium 200 mg, Cyanocobalamin (Vitamin B12) 12	One tablet orally daily

		mcg, Folic Acid (Vitamin B9) 1 mg, Pyridoxine (Vitamin B6) 75 mg	
(b) (4)	Look	Injection, solution: 0.1 mL/dose (1 mL)	(b) (4)
Comtan (entacapone)	Look	Tablets: 200 mg	200 mg with each dose of levodopa/carbidopa, up to a maximum of 8 times/day (maximum daily dose: 1600 mg/day).
Aredia (pamidronate)	Look	Injection, powder for reconstitution: 30 mg, 90 mg Injection, solution: 3 mg/mL (10 mL); 6 mg/mL (10 mL); 9 mg/mL (10 mL)	60-90 mg, as a single dose over 2-24 hours, repeated after 2-3 weeks or up to 2-3 months as needed. Paget's Disease: 30 mg intravenously over 4 hours daily for 3 consecutive days
Camolea (herbal-mezeron bark)	Look	Bark compounded into 20% ointment	Dose unknown. Mezereon is a protected species and is seldom used medicinally anymore.
Cambogia (Garcinia Cambogia herbal-fruit rind)	Look	Compounded into extract	For weight loss, an extract containing 50% hydroxycitric acid, 1000 mg three times daily has been used. Hydroxycitric acid, 500 mg four times daily has also been used for weight loss
Coumadin (warfarin)	Look	Tablets: 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, 10 mg	One tablet orally daily. Adjust dose according to INR results; usual maintenance dose ranges from 2-10 mg daily.
Campath (alemtuzumab)	Look	Injection, solution: 30 mg/ 1 mL	Via intravenous infusion): Initial: 3 mg/day beginning on day 1; when tolerated (no grade 3 or 4 infusion

			reactions), increase to maintenance dose of 30 mg/dose 3 times/week on alternate days for a total duration of therapy of up to 12 weeks. Maximum dose/day: 30 mg; maximum cumulative dose/week: 90 mg Pretreatment (with acetaminophen and an oral antihistamine) is recommended
(b) (4)			
(b) (4)			
Avandia (rosiglitazone)	Look and Sound	Tablets: 2 mg, 4 mg, 8 mg	4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 8-12 weeks, the dosage may be increased to 8 mg daily in single or in divided doses twice daily.

Appendix G: Potential confusing name

Cambia **(diclofenac potassium) for oral solution**	**50 mg**	**One packet (50 mg) mixed in 30-60 mL of water and then ingested**
Failure Mode: **Name confusion**	**Causes** **(could be multiple)**	**Effects**
Cancidas (caspofungin)	Look Injection, Powder for reconstitution: 50 mg and 70 mg 70 mg via intravenous infusion over one hour on day one, followed by **50 mg** daily thereafter	Orthographic differences in the names minimize the likelihood of medication errors in the usual practice setting. Specifically the letter 's' at the end of Cancidas differentiates the name and the name Cancidas is notably longer than the name Cambia. Cancidas is a different dosage form (powder for injection) than Cambia (powder for oral solution). Cancidas and Cambia have overlapping numerical strengths and doses (50 mg) that can increase the potential for confusion. However, Cambia is an oral pain reliever that is administered as a single dose on an as needed basis for migraine headache, whereas Cancidas is an injectable antifungal agent administered every day in critically ill hospitalized patients. Due to orthographic differences, as well as differences in the dosing frequency, indication, length of treatment and area of use, DMEPA believes it is unlikely that a medication error will occur.
Cantil (mepenzolate bromide)	Look Tablets: 25 mg 1 or 2 tablets (25 mg or **50 mg**) 4 times a day preferably with meals and at bedtime.	Orthographic differences in the names minimize the likelihood of medication errors in the usual practice setting. Specifically the letter 'l' at the end of Cantil creates an upstroke and the letter 't' as vertically crossed when scripted will differentiate the name from Cambia. Cantil and Cambia have an overlapping dose (50 mg) and a shared route of administration (oral) that can increase the potential for confusion. However, Cambia is administered as a single dose on an as needed basis for migraine headache, whereas Cantil 50 mg is administered as two 25 mg tablets four times a day on a daily scheduled basis. The indications differ as well (migraine headaches versus peptic ulcer). Due to orthographic differences, as well as differences in the dosing frequency, indication, and length of treatment, DMEPA believes it is unlikely that a medication error will occur.
Camila (norethindrone)	Look Tablets: 0.35 mg (28 count)	Although the names Camila and Cambia look similar when scripted, different product characteristics and packaging will decrease the potential for confusion.

	1 tablet daily	Camila and Cambia have different strengths (0.35 mg vs. 50 mg), and since they are each available in a single strength, the strength may be omitted from a prescription. Camila and Cambia are also available in different package sizes (28 count oral contraceptive package vs. 9 count packets), and this information may also be omitted on a prescription. However, Camila and Cambia have different dosing frequencies which will help differentiate the products when included on a prescription (single dose as needed vs. once daily). Furthermore, Camila's distinctive packaging as an oral contraceptive and Cambia's packet packaging, will be obvious to a user in the unlikely event that an error occurs.

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